

Breaking Barriers: Unraveling the Past, Paving the Future – Rethinking Pulmonary Function Tests Beyond Race

UCSF



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Learning objectives

- Describe how race was historically imbedded in PFT interpretation.
- Identify nongenetic determinants of lung function that might contribute to racial differences in lung growth and functional decline.
- Evaluate race-specific PFT interpretation and how this approach might lead to health disparities.
- Articulate the rationale for race-neutral PFT interpretation.
- Assess the many remaining gaps in our understanding of how to use pulmonary function tests to improve health.

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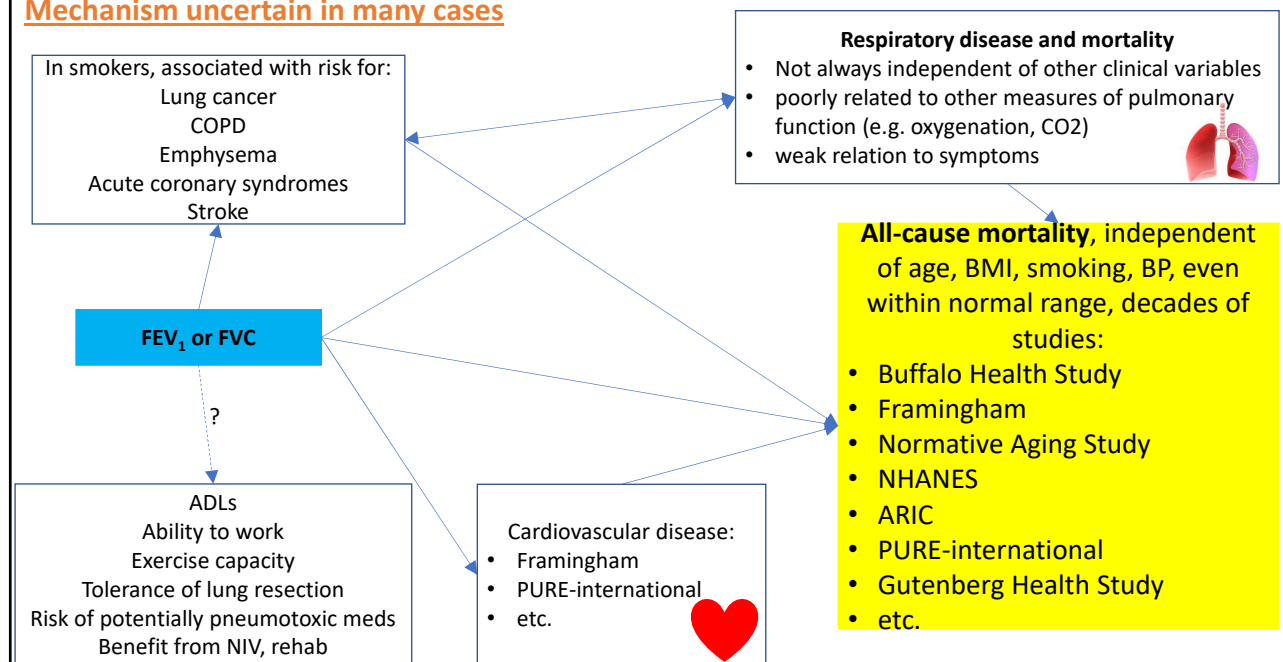
Spirometry

- **Quantify volume and flow of air moving in and out of lungs**
- **FEV₁**: maximum volume of air forcefully exhaled within one second from a full inhalation
- **FVC**: volume of air that can be forcefully exhaled all the way from full inspiration to full exhalation
- **FEV₁/FVC**: we look at the ratio value, not what it is as a % of predicted.



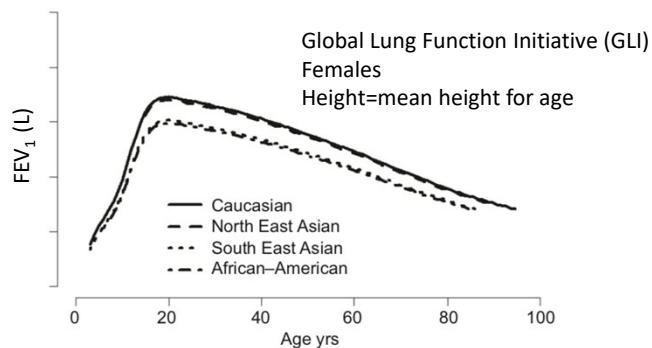
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Statistical associations of FEV₁ and FVC with health Mechanism uncertain in many cases



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The race-specific approach to pulmonary function



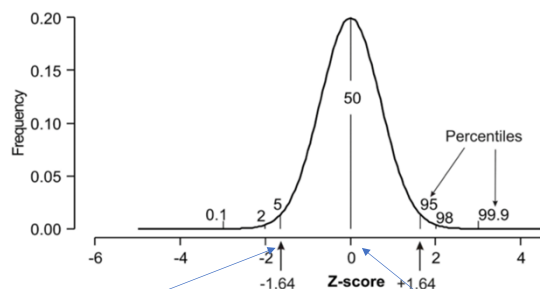
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47-year-old female
5'5" (165.1 cm)
Measured FEV₁ 2.0 L

GLI African-American Predicted FEV₁ 2.53 L

- 79% of predicted, z -1.46
- 2.0 > lower limit of 1.93 L



Lower limit of normal, 5th percentile

Predicted value

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Conclude: Normal

GLI White Predicted FEV₁ 2.94 L

- 68% of predicted, z -2.43
- 2.0 < lower limit of 2.31 L

Conclude: Abnormal

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47-year-old female
5'5" (165.1 cm)
Measured FEV₁ 2.0 L

GLI African-American Predicted FEV₁ 2.53 L

GLI White Predicted FEV₁ 2.94 L

THIS DECISION WE CREATED HAS REAL IMPLICATIONS

- Will respiratory disease be considered? Additional tests done?
- Referral for lung transplantation evaluation?
- Denied lung cancer resection?
- Eligible for disability?
- Eligible to work as a firefighter or diver?

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Challenges with race

- Not uniformly defined across time and location
- Can mask modifiable risks for reduced lung function and disease
- Not a proxy for genetics: variation in genome within races categories is large
- Limited categories and they do not account for effects of acculturation and mixed backgrounds
- Residual differences in lung function between race categories were used to justify an idea of innate inferiority



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Understanding the ATS Process



- 2019: Momentum to critically examine the use of race in clinical algorithms was building alongside increased attention on race and racism in our society.
- In 2020, a few members of the ATS Committees on Pulmonary Function Testing and on Health Equity and Diversity identified a need for a workshop and invited a diverse group of participants.

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AMERICAN THORACIC SOCIETY DOCUMENTS

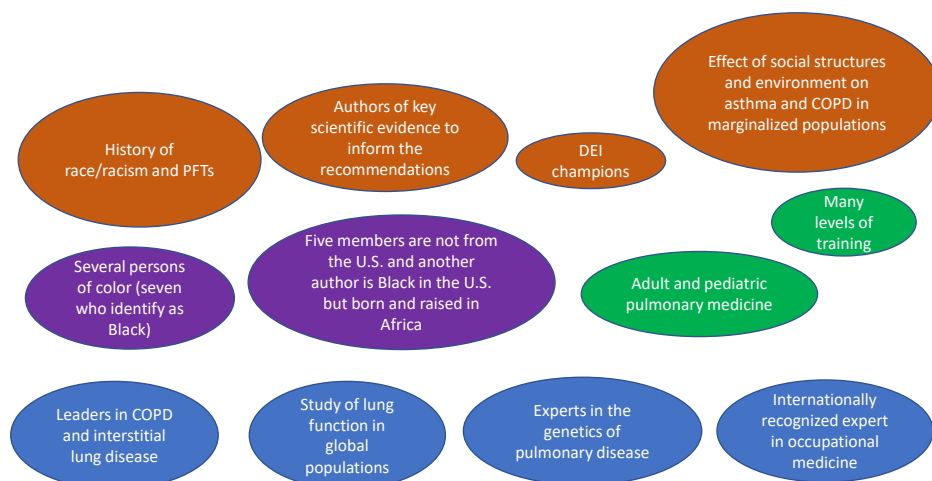
Race and Ethnicity in Pulmonary Function Test Interpretation An Official American Thoracic Society Statement

Nirav R. Bhakta, Christian Bime, David A. Kaminsky, Meredith C. McCormack, Neeta Thakur, Sanja Stanojevic, Aaron D. Baugh, Lundy Braun, Stephanie Lovinsky-Desir, Rosemary Adamson, Jonathan Witonsky, Robert A. Wise, Sean D. Levy, Robert Brown, Erick Forno, Robyn T. Cohen, Meshell Johnson, John Balmes, Yolanda Mageto, Cathryn T. Lee, Refiloe Masekela, Daniel J. Weiner, Charlie G. Irvin, Erik R. Swenson, Margaret Rosenfeld, Richard M. Schwartzstein, Anurag Agrawal, Enid Neptune, Juan P. Wisnivesky, Victor E. Ortega, and Peter Burney; on behalf of the American Thoracic Society Committees on Pulmonary Function Testing and on Health Equity and Diversity

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS FEBRUARY 2023 AND ENDORSED BY THE EUROPEAN RESPIRATORY SOCIETY MARCH 2023

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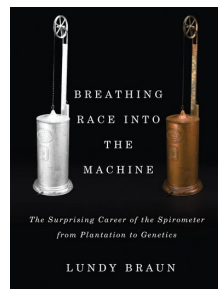
Diversity and expertise: 33 members



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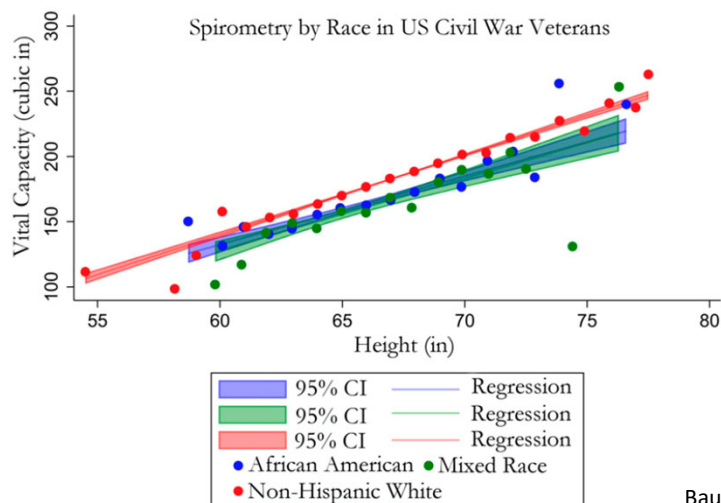
History: race-centric, biased, unquestioned

- Views that racial categories reflected innate characteristics drove the organization of pulmonary function observations while ignoring other factors.
- Disproportionate emphasis on race limited understanding of determinants of pulmonary function.
- Majority of research that formed the evidence base for lower lung function in non-White populations did not examine socioeconomic status (Braun ERJ 2013).
- Physiologists justified race from differences in the ratio of limb length to chest height, but this view is:
 - Quantitatively insufficient
 - Expected to reflect the environment, ≠ all innate



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Racial differences may be as much social as genetic in origin: reanalysis of Gould's data

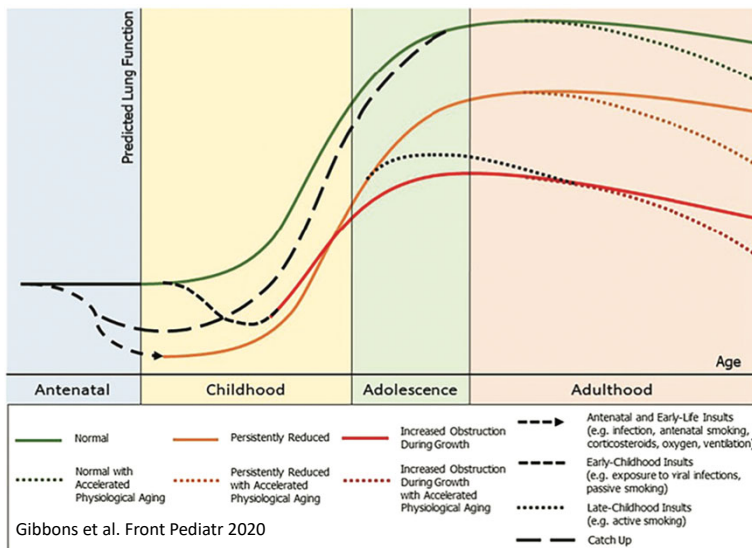


Baugh AD et al. Annals ATS. 2023

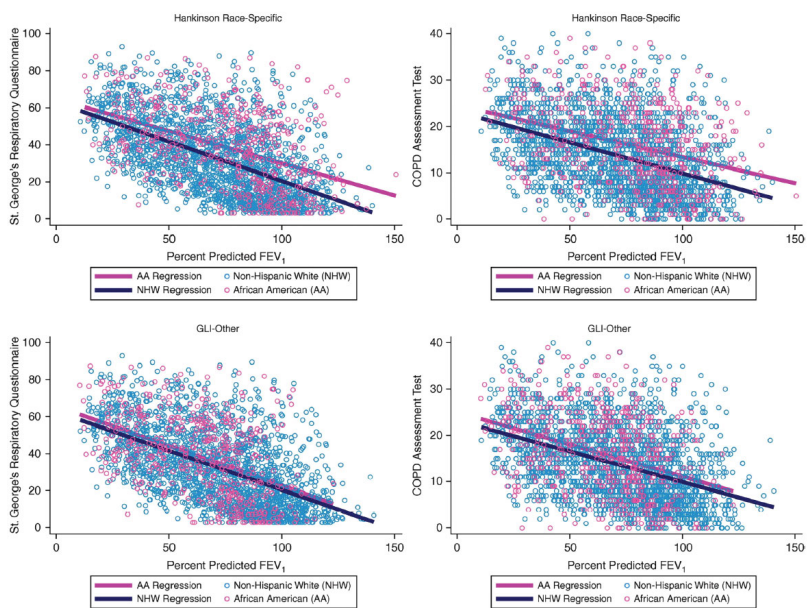
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Determinants of pulmonary function

- Early-life
- Prematurity
- Infections
- Nutrition: over and under
- Second-hand smoke
- Indoor/outdoor pollution
- Discrimination, stress
- Genetics
 - Genetic ancestry vs
 - SNPs



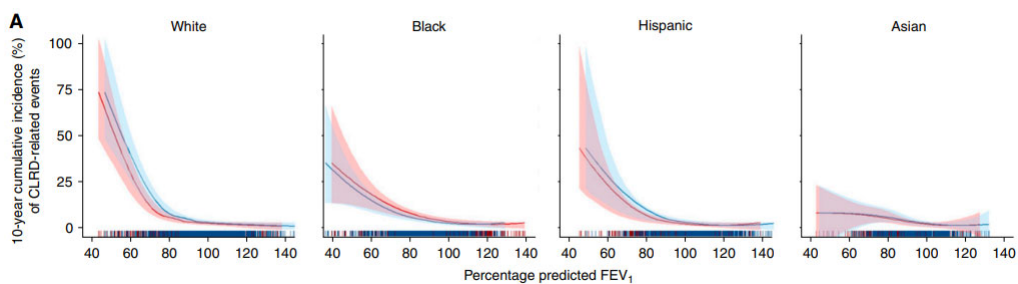
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Baugh et al. AJRCCM 2022

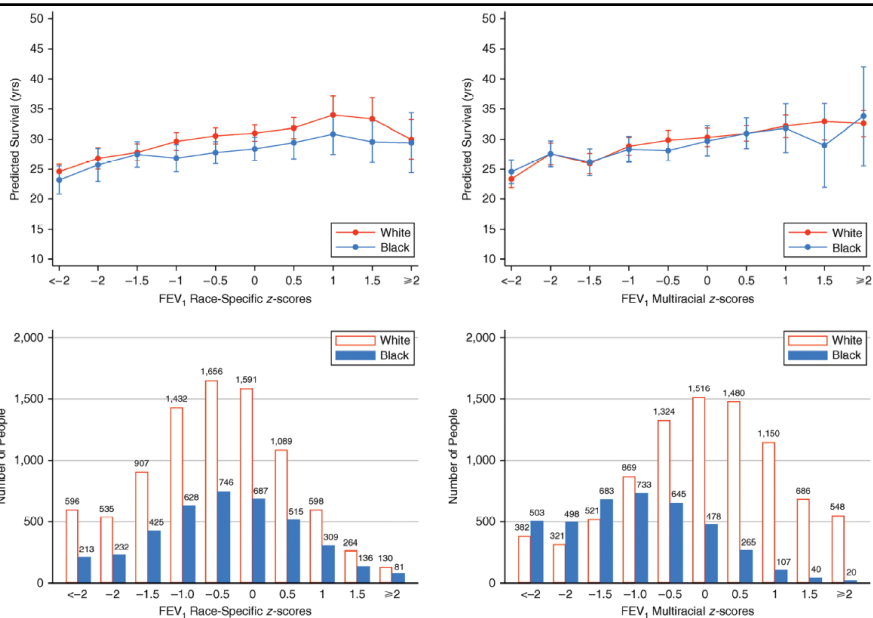
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General Population Evidence



Elmaleh-Sachs et al. AJRCCM 2022

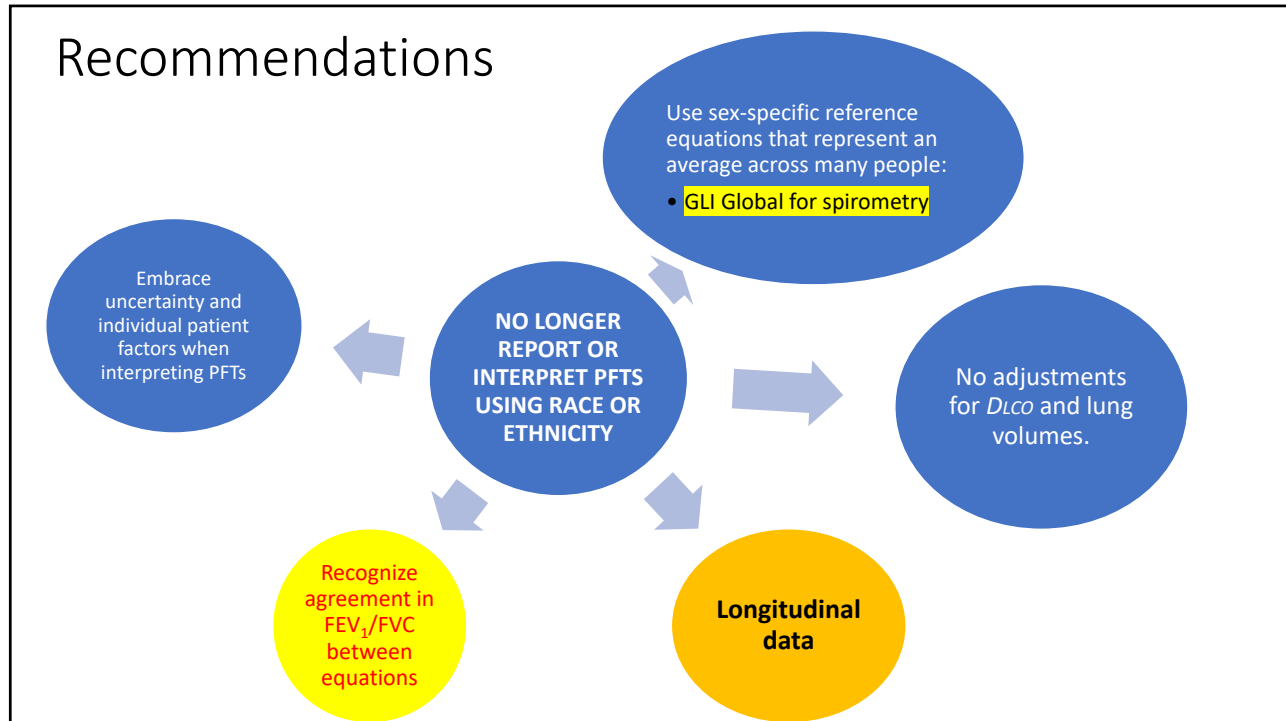
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McCormack et al. AJRCCM 2022

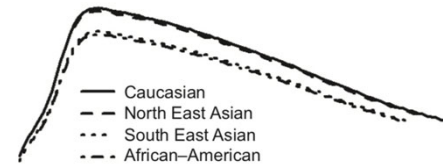
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Recommendations



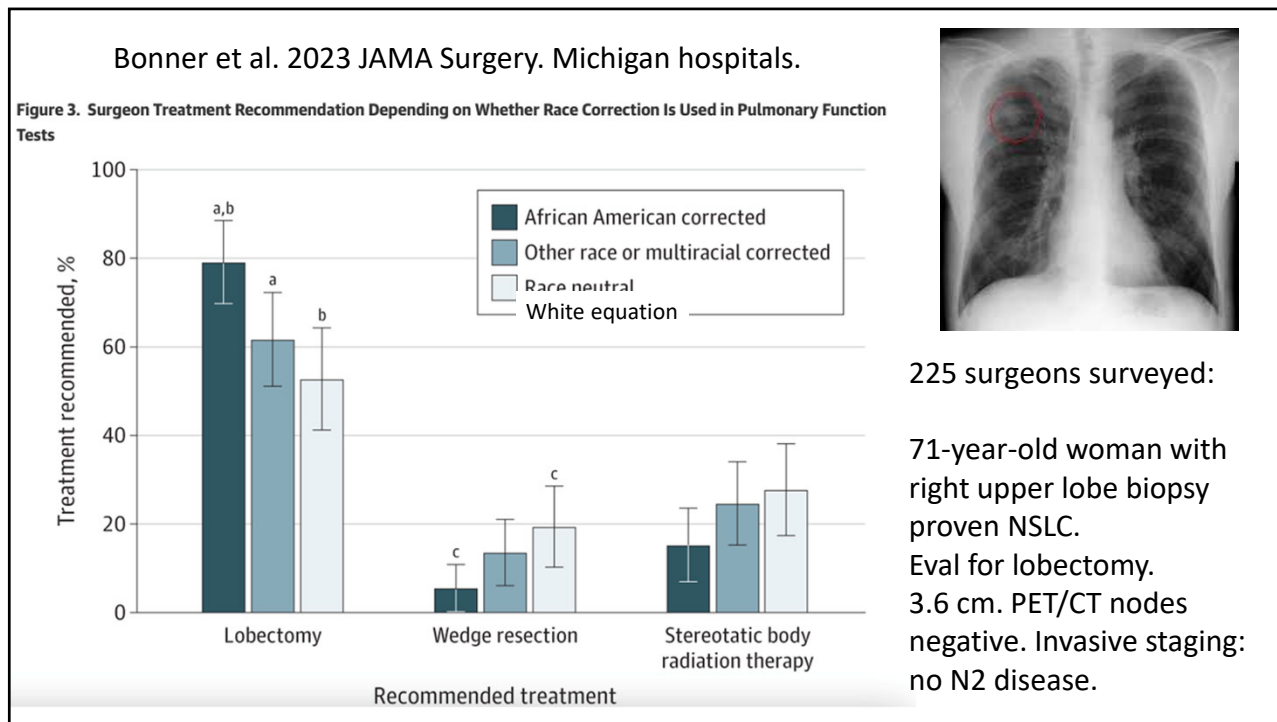
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Clinical implications

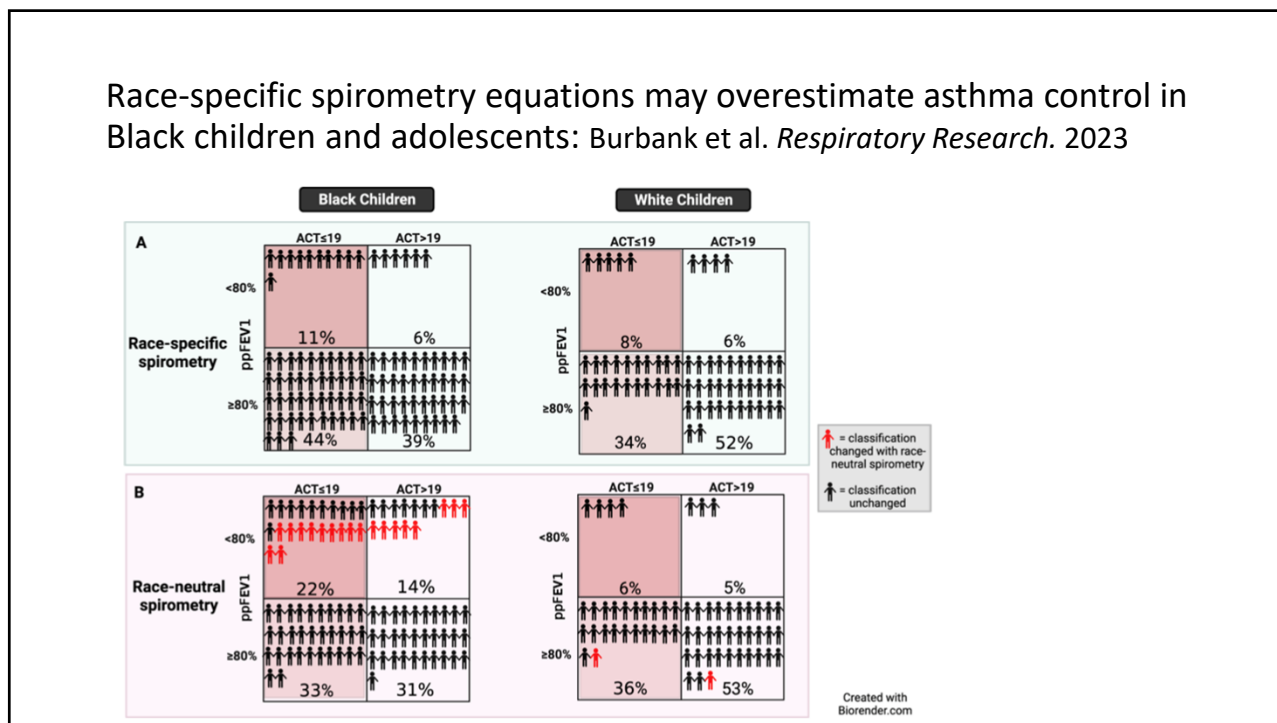


- In most cases, GLI Global shifts the mean predicted value and lower limit of normal to values that are:
 - Higher compared to African American and South East Asian equations
 - Lower compared to White and North East Asian equations
- Thus, application of GLI Global yields relative values (z scores and % of predicted) that are:
 - Lower compared to African American and South East Asian equations
 - Higher compared to White and North East reference equations
- FEV_1/FVC has relatively minor variation between equations

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Implementation factors

- Software updates, availability, cost
- Prevent trending of relative values in the electronic health record across a change in reference equations, interoperability
- Speaking to patients and colleagues:
 - concerns about impact on White persons
 - Black persons' employment
 - dispelling a misconception of precision from using race
- Continue to engage with the many users of PFTs external to clinical medicine, for example:
 - Disability evaluation (AMA guidelines)
 - occupational evaluation
 - life insurance

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Remaining challenges

- Ideal composition of reference population uncertain: does location matter?
- Need for reference equations uncertain: absolute FEV₁, FEV1Q
- Decreasing value of normalized FEV₁, FVC, TLC, DLCO in the era of increased availability of others tests (CT, TTE, V/Q, right-heart cath)
- What the right amounts of FEV₁, FVC, TLC, and DLCO are for body size, task, or exposure are poorly understood.
- Thresholds to make decisions from PFTs are largely not evidence-based
 - Need to anchor use of PFTs on patient-centered outcomes rather than normal vs abnormal.
- Race and ethnicity categories have a role in understanding impact of structural racism on lung health and function

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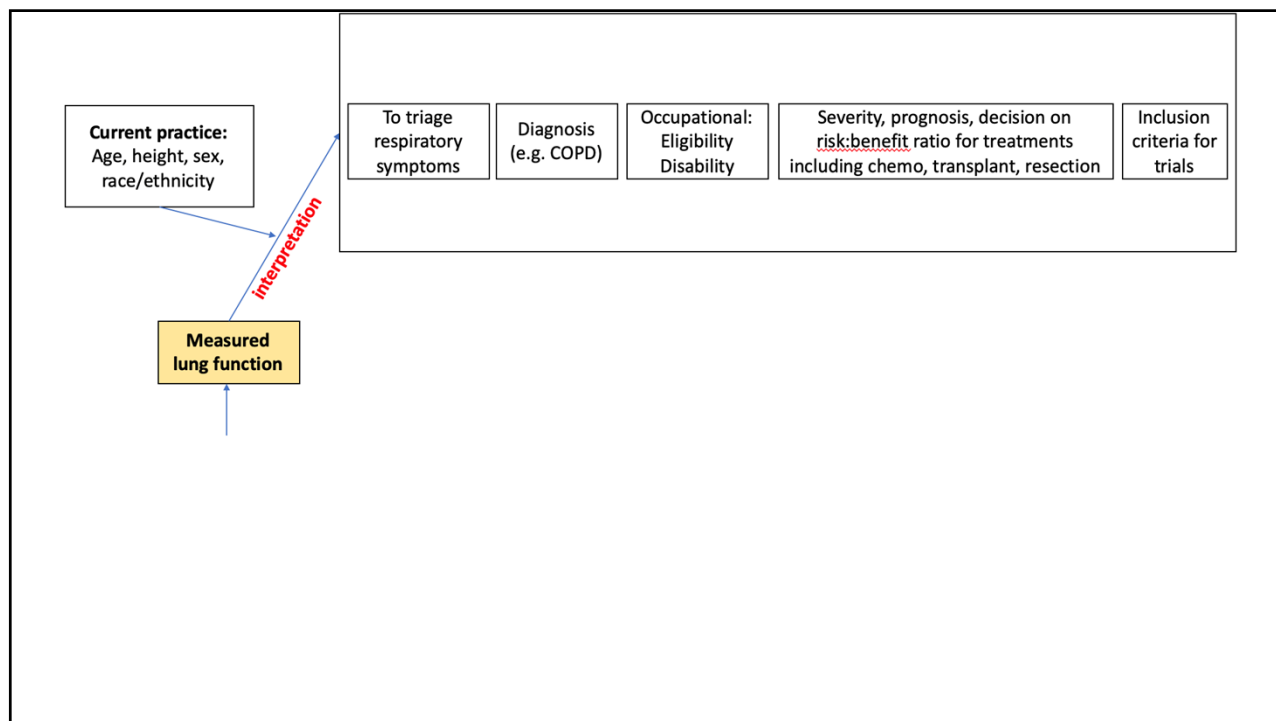
THE JOURNEY MUST CONTINUE

Acknowledgments

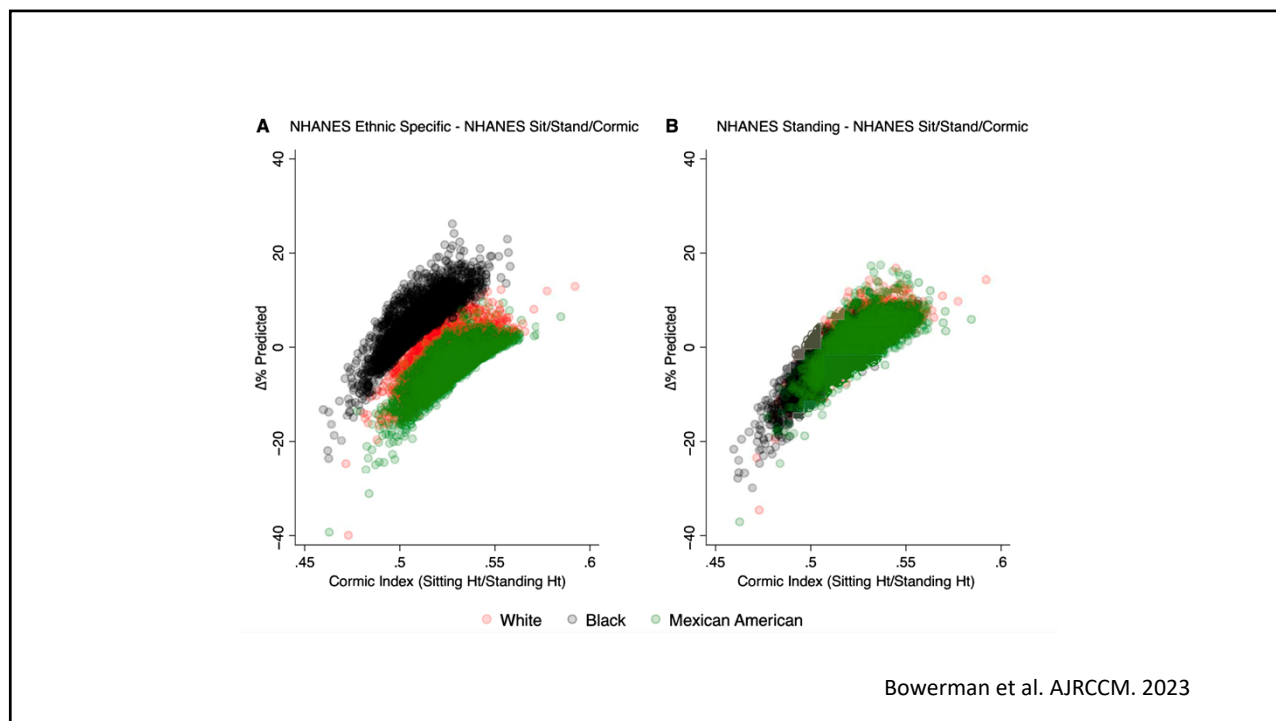
Christian Bime
 Workshop members
 ATS Executive Committee



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The Contribution of Anthropometry and Socioeconomic Status to Racial Differences in Measures of Lung Function

A Systematic Review

Rachel Holland, BSc; Cole Bowerman, MSc; and Sanja Stanojevic, PhD

[Check for updates](#)

BACKGROUND: The current approach to interpretation of lung function measurements assumes that differences in lung function between racial and ethnic groups represent inherent and biological differences. Observed differences in lung function between White and Black populations are often attributed to physiological differences in body proportions (eg, chest size, leg length); however, most studies investigating the observed differences have not considered the impact of socioeconomic status (SES).

RESEARCH QUESTION: What proportion of the differences in lung function between Black and White populations can be attributed to SES and/or differences in body proportions?

STUDY DESIGN AND METHODS: PubMed and EMBASE were searched up to March 2022 for articles relating to Black race, SES, and lung function. A total of 4,673 titles and abstracts were screened, followed by assessment for extractable data; 11 articles were ultimately included in this systematic review.

RESULTS: There is substantial heterogeneity in the contribution of SES and body proportions to the observed differences in lung function between Black and White individuals. The proportion of differences between Black and White study participants attributable to SES factors ranged from 2.2% to 43.3% in FEV₁ and from 4.1% to 41.9% for FVC. Studies that adjusted for sitting height explained 3% to 31.7% of the racial difference in lung function.

INTERPRETATION: Reproducible research aimed at explaining the etiology of the differences in lung function between populations is difficult to achieve. The evidence to support the use of race/ethnic specific equations is limited, and the practice needs to be re-evaluated.

CHEST 2022; 162(3):635-646

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A 55-year-old man with COPD is found to have a right hilar mass. The mass undergoes biopsy and pathology reveals squamous cell carcinoma. The patient undergoes spirometry for evaluation of potential pneumonectomy.

What is the expected change in the reported relative values (e.g., z-score and percentage of predicted) after a switch from the NHANES III or GLI African American reference equations to the average race-composite GLI Global reference equations?

- A. Increase in percent predicted FEV1, FVC, and FEV1/FVC
- B. Increase in percent predicted FEV1 and FVC. Decrease in FEV1/FVC.
- C. Decrease in percent predicted FEV1, increase in percent predicted FVC, and decrease in FEV1/FVC
- D. Decrease in percent predicted FEV1 and FVC. No change in FEV1/FVC
- E. Not enough information. The patient's race needs to be specified

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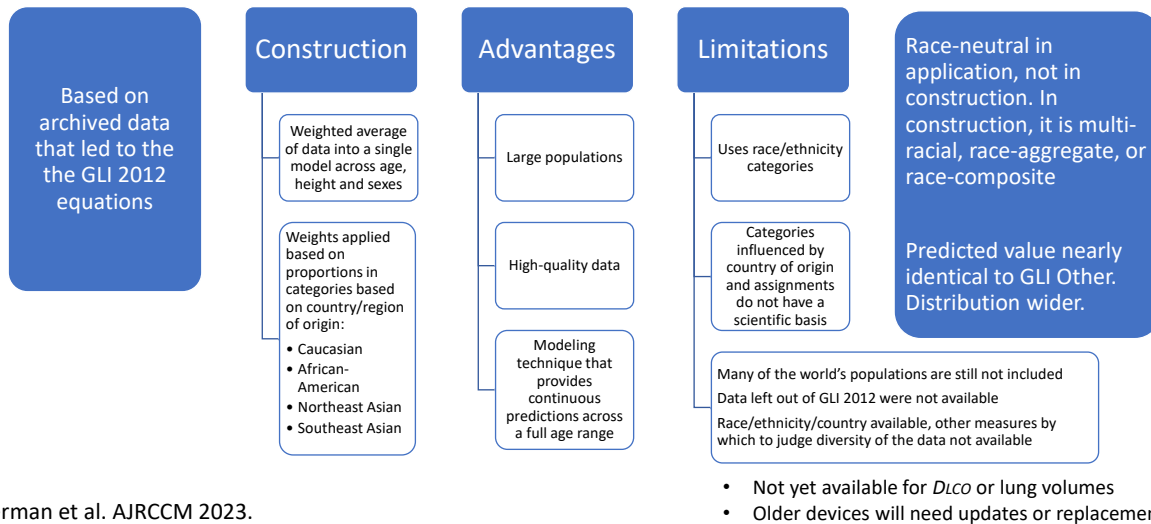
What is the expected change in the reported relative values (e.g., z-score and percentage of predicted) after a switch from the NHANES III or GLI African American reference equations to the average race-composite GLI Global reference equations?

Correct Answer:

D. Decrease in percent predicted FEV1 and FVC. No change in FEV1/FVC

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GLI Global



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Lung function vs other tests in medicine

• Differences between eGFR and PFTs:

- There are established differences in lung function between races
- PFTs are an actual measurement of lung function rather than an estimation through an intermediate (e.g., creatinine).
- eGFR is not reported as a relative value: z scores and % predicted.
- No equivalent of cystatin C or iothalamate clearance for PFTs.
- As with lung function, we expect GFR to vary with body size, but in pulmonary we make greater efforts to adjust for (eGFR is reported as per 1.73 m² BSA).
- Other measures to assess function do not depend on size (e.g., TSH/T4, AST, WBC, LVEF, bone density).
- A better analogy to outputs from other organs are PaO₂ and PaCO₂—their relationship to PFTs is weak. FEV₁/FVC is closest to other outputs as it is independent of height and varies little between racial/ethnic backgrounds.
- What the right amount of FEV₁, FVC, TLC, and DLCO is for body size and task/exposure is poorly understood.
- Decreasing value of normalized FEV₁, FVC, TLC, DLCO in the era of widespread availability of others tests (CT, TTE, V/Q, cath).
- Trends in absolute lung function often most important.

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Questions?